Remarks

Applicants have amended the title to reflect the subject matter of the pending claims. Applicants amended the paragraph on page 7 to correct a typographical error. In particular, the references for the amino acid sequences of BCMA and BR43X1 have been revised from SEQ ID NOs: 6 and 7 to SEQ ID NOs: 8 and 9, respectively. Support for this amendment can be found in Figure 1, and throughout the specification (*e.g.*, at page 52, second paragraph).

Applicants have canceled claims 1 to 63, and Applicants have added claims 63 to 96, leaving claims 63 to 96 pending in the present application. Applicants canceled claims 2, 3, 5 to 8, and 29 to 63 in view of the election of claims designated "Group II" by the Examiner. The cancellation of these claims necessitated the deletion of Wenfeng Xu, Karen Madden, and David P. Yee as named inventors.

The new claims are focused upon particular aspects of the invention designated Group II in light of commercial considerations. Applicants reserve the right to pursue claims directed to the subject matter of canceled claims in continuation and divisional applications.

Support for claims 64 and 65 can be found at least in original claim 1. Support for the term "BlysS" in claims 64, 72, 73, 81, and 93 can be found, for example, on page 2 (first full paragraph), page 14 (third paragraph), and page 103 (last paragraph), which discloses that the TACI ligand "ztnf4" is also known as "BLyS." Support for claims 66 to 71, 75 to 80, and 87 to 92 can be found at least on page 2 (last paragraph) through page 3 (first paragraph). Support for claims 72, 81, and 93 can be found at least in original claim 13 and on page 53 (first full paragraph). Support for claims 73 and 74 can be found at least in original claim 4. Support for claims 82, 83, 84, 94, and 95 can be found at least on page 45, last paragraph. Support for claims 85, 86, and 96 can be found at least in Example 6.

No new matter has been added by way of these amendments.

Applicants have attached a marked-up version of the changes made to the application by the present amendment. The attached pages are captioned "Version with Markings to Show Changes Made."

Conclusion

If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6681.

Respectfully submitted,
ZymoGenetics, Inc.

Phillip B. C. Jones
Registration No. 38,195

Version with Markings to Show Changes Made

In the Application:

Wenfeng Xu, Karen Madden, and David P. Yee were deleted as named inventors.

In the Specification:

The title at line 6 of page 1 has been amended as follows: ~~SOLUBLE RECEPTOR BR43X2 AND METHODS OF USING~~ METHODS FOR INHIBITING BLyS ACTIVITY WITH TACI POLYPEPTIDES

The paragraph beginning at line 5 of page 7 has been amended as follows:

Figure 1 shows a multiple amino acid sequence alignment between BR43x2, TACI (von Bülow and Bram, ibid.) (SEQ ID NO:6), BCMA (Gras et al., ibid.) (SEQ ID NO:~~6~~8) and BR43x1 (SEQ ID NO:~~7~~9). The cysteine-rich pseudo repeats and transmembrane domain are noted.

In the Claims:

Claims 1 to 63 have been canceled.

Claims 64 to 96 have been added by amendment. The new claims are:

--64. A method of inhibiting BLyS activity in a mammal comprising administering to the mammal a composition comprising a transmembrane activator and calcium-modulator and cyclophilin ligand-interactor (TACI) polypeptide, wherein the TACI polypeptide comprises an extracellular domain of TACI, wherein TACI has an amino acid sequence consisting of SEQ ID NO:6, and wherein the TACI polypeptide binds BLyS.

65. The method of claim 64, wherein the TACI polypeptide consists of an extracellular domain of TACI.

66. The method of claim 64, wherein the TACI extracellular domain comprises amino acid residues 25 to 104 of SEQ ID NO:6.

67. The method of claim 66, wherein the TACI extracellular domain consists of amino acid residues 25 to 104 of SEQ ID NO:6.

68. The method of claim 66, wherein the TACI extracellular domain comprises amino acid residues 1 to 154 of SEQ ID NO:6.

69. The method of claim 68, wherein the TACI extracellular domain consists of amino acid residues 1 to 154 of SEQ ID NO:6.

70. The method of claim 66, wherein the TACI extracellular domain comprises amino acid residues 1 to 166 of SEQ ID NO:6.

71. The method of claim 70, wherein the TACI extracellular domain consists of amino acid residues 1 to 166 of SEQ ID NO:6.

72. The method of claim 64, wherein the BLyS activity is antibody production, and wherein administration of the composition inhibits antibody production.

73. A method of inhibiting BLyS activity in a mammal comprising administering to the mammal a composition comprising a fusion protein consisting of a first portion and a second portion, wherein the first portion and second portion are joined by a peptide bond, wherein the first portion comprises an extracellular domain of the transmembrane activator and calcium-modulator and cyclophilin ligand-interactor (TACI), wherein TACI has an amino acid sequence consisting of SEQ ID NO:6, and wherein the fusion protein binds BLyS.

74. The method of claim 73, wherein the first portion consists of an extracellular domain of TACI.

75. The method of claim 73, wherein the TACI extracellular domain comprises amino acid residues 25 to 104 of SEQ ID NO:6.

76. The method of claim 75, wherein the TACI extracellular domain consists of amino acid residues 25 to 104 of SEQ ID NO:6.

77. The method of claim 75, wherein the TACI extracellular domain comprises amino acid residues 1 to 154 of SEQ ID NO:6.

78. The method of claim 77, wherein the TACI extracellular domain consists of amino acid residues 1 to 154 of SEQ ID NO:6.

79. The method of claim 75, wherein the TACI extracellular domain comprises amino acid residues 1 to 166 of SEQ ID NO:6.

80. The method of claim 79, wherein the TACI extracellular domain consists of amino acid residues 1 to 166 of SEQ ID NO:6.

81. The method of claim 73, wherein the BLyS activity is antibody production, and wherein administration of the composition inhibits antibody production.

82. The method of claim 73, wherein the composition comprises a multimer of fusion proteins.

83. The method of claim 82, wherein the composition comprises a dimer of fusion proteins.

84. The method of claim 73, wherein the second portion of the fusion protein is an immunoglobulin heavy chain constant region.

85. The method of claim 84, wherein the immunoglobulin heavy chain constant region is a human immunoglobulin heavy chain constant region.

86. The method of claim 85, wherein the human immunoglobulin heavy chain constant region is a human immunoglobulin heavy chain constant region of IgG1.

87. The method of claim 85, wherein the TACI extracellular domain comprises amino acid residues 25 to 104 of SEQ ID NO:6.

88. The method of claim 87, wherein the TACI extracellular domain consists of amino acid residues 25 to 104 of SEQ ID NO:6.

89. The method of claim 87, wherein the TACI extracellular domain comprises amino acid residues 1 to 154 of SEQ ID NO:6.

90. The method of claim 89, wherein the TACI extracellular domain consists of amino acid residues 1 to 154 of SEQ ID NO:6.

91. The method of claim 87, wherein the TACI extracellular domain comprises amino acid residues 1 to 166 of SEQ ID NO:6.

92. The method of claim 91, wherein the TACI extracellular domain consists of amino acid residues 1 to 166 of SEQ ID NO:6.

93. The method of claim 87, wherein the BLyS activity is antibody production, and administration of the composition inhibits antibody production.

94. The method of claim 87, wherein the composition comprises a multimer of fusion proteins.

95. The method of claim 94, wherein the composition comprises a dimer of fusion proteins.

96. The method of claim 87, wherein the human immunoglobulin heavy chain constant region is a human immunoglobulin heavy chain constant region of IgG1.--